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09/786,998	06/14/2001	Maria Adele Pacciarini	01-270	1122

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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT PAPER NUMBER

1623

DATE MAILED: 05/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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DETAILED ACTION

The amendment filed 3/3/2005 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-12 and 15-17 have been canceled.
2. New Claims 20-31 have been added.
3. Claims 18-19 have been amended.
4. Remarks drawn to rejections under 35 USC 103

Claims 13-14 and 18-31 are pending in the case.

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

The finality of the previous office action mailed 8/26/2004 has been withdrawn as per the Interview Summary of 9/25/2005.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 13-14 and 18-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bargiotti et al (US 5,304,687) in combination with Kuhl et al (Cancer Chemother. Pharmacol., 1993, 33, 10-16), Nakamura et al (Gan. To Kagaku Ryoho 1988, Aug. 15 (8 Pt 2), 2562-7,

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English Abstract) and Gorbunova (Intrahepatic Arterial Infusion Chemotherapy for Primary and Metastatic Cancer of the Liver, 1990).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Bargiotti et al, drawn to morpholino derivatives of anthracyclines teach methoxy morpholino doxorubicin (col. 1, lines 10-62; compounds A4 and A5). These derivatives are shown to inhibit solid tumors such as human carcinoma with intravenous and oral route (col. 11, lines 62-68; col. 12, Table 6). However, the intrahepatic route of administration is not specifically taught.

Kuhl, drawn to doxorubicin derivatives, teaches that the methoxymorpholino derivative of doxorubicin has a broad-spectrum antitumor activity and is non-cross-resistant in multi drug

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tumor resistant models. It is also activated in the liver to a metabolite which crosslinks to DNA and is 10 times more potent (Abstract, page 10).

Nakamura et al teach that intra-arterial infusion of lipiodol (iodized oil) and adriamycin (same as doxorubicin) showed remarkable therapeutic effects for advanced cancer (English abstract).

Gorbunova teaches in general that intra hepatic arterial infusion chemotherapy allows for creating a super high concentration of an antitumor agent in the organ affected by the tumor (English abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising methoxymorpholino doxorubicin with iodized oil and use the same in a method of treating a human liver tumor and reducing systemic exposure as instantly claimed since such is seen to be taught in the prior art. It is well within the purview of one of ordinary skill in the art to adjust dosages and the frequency of administration based on that taught in the prior art.

One of ordinary skill in the art would have been motivated to use MMDX in hepatic artery administration since prior art recognizes that hepatic artery administration of doxorubicin is beneficial in treating tumor and reducing systemic exposure. Hepatic arterial administration also creates super high concentrations in the organ affected. This localized administration is beneficial for reducing systemic exposure and reducing tumor volume in the liver.

Conclusion

Claims 12-13 and 18-31 are rejected

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

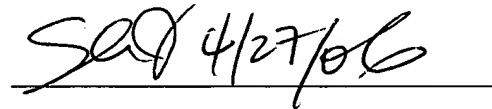
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK

A handwritten signature in black ink, appearing to read 'SJJ 4/27/06', is written over a horizontal line.

Shaojia Jiang
Supervisory Patent Examiner
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